

### REMARKS

After entry of the above-described amendments, claims 106-114, 116-124, 126-133, and 135-139 will be pending.

Claims 106-136 were previously pending in this application. Claims 130-133, 135 and 136 have been amended to correct an obvious typographical error in claim dependency. Claims 106, 118 and 127 have been amended with this Action. Support for these amendments can be found throughout the application as filed, for example at page 2, lines 36-37, page 3, lines 9-10, page 4, lines 35-38, page 7, lines 1-2, and at page 7, line 38 to page 8, line 4, as well as in the further explanation provided below. Claims 115, 125 and 134 have been canceled and new claims 137-139 have been added. Support for new claims 137-139 can be found throughout the application as filed and in previously presented claims 106, 115, 118, 125, 127 and 134, as well as in the above-cited portions of the specification supporting the amendments to claims 106, 118 and 127. Accordingly, no new matter has been added with these amendments.

The outstanding rejections will be addressed separately below.

### New Matter

The Advisory Action dated February 12, 2007 states that “[t]he proposed amendment adds the limitation “regional-identity unrestricted pluripotent” which would be rejected as new matter...(because)...[t]he specification does not teach that the neural precursor cells are unrestricted or pluripotent...(and)...”does not define “regional-identity” or provide implicit support for “regional-identity” and any physical or functional properties intended to be associated with said regional-identity.

In response, Applicants respectfully aver that the indicated language is not new matter, because it is a limitation that is intrinsically supported by the teachings of the specification as would be readily recognized by one of skill in the art. Indeed, Applicants note that the “pluripotent” nature of embryonic stem cells, as well as the embryonic stem cell-derived neural precursors, and neuronal or glial cells derived from the embryonic stem cell-derived neural precursor cells, is described throughout the application as filed, as further detailed above. The

well-known and commonly accepted definition of pluripotent is defined in Applicants' specification as "[p]recursor cells which have the potential to differentiate into many different...mature cell types" (specification at page 7, lines 35-36). In further clarification, the specification states that "[i]n neurobiology, bipotential cells are frequently used as a term for precursor cells which can generate astrocytes and oligodendrocytes" (specification at page 7, lines 36-38). The presence of non-pluripotent neuronal or glial cell cells in a pluripotent cell composition that includes pluripotent embryonic stem cell-derived neural precursors does not make the cell composition non-pluripotent. The presence of the pluripotent cells in the claimed composition makes the claimed composition a pluripotent one. Accordingly, the pluripotent nature of the cell compositions of the invention comprising embryonic stem cell-derived neural precursors, and neuronal or glial cells derived from the embryonic stem cell-derived neural precursor cells, would be understood by a person of ordinary skill in the art.

Furthermore the "regional-identity unrestricted" nature of the claimed cell compositions is inherent to the teachings of the specification as filed, as fully attested to in the Second Declaration of Dr. Bruestle. Applicants respectfully note that there is no *ipsis verbis* requirement for written description (see MPEP § 2163 (II.) (A.) (3.) (a.)), and that new or amended claims may be "supported in the specification through express, implicit or inherent disclosure" (emphases added, see MPEP § 2163 (I.) (B.)). Furthermore, new claims 137, 138 and 139, which contain the same "regional-identity unrestricted, pluripotent" language, are fully supported by the application as filed for the same reasons as well.

Accordingly, Applicants respectfully aver that these proposed amendments and new claims present no issue of new matter because the regional-identity unrestricted nature of the claimed cell compositions would be understood by one of skill in the art as intrinsically or inherently present in the claimed cell compositions.

**Rejections under 35 U.S.C. §112, 1<sup>st</sup> paragraph**

Claims 115, 125 and 134 were rejected under 35 U.S.C. §112, first paragraph, "for reasons of record set forth in the Office Actions of 4/21/04 and 12/2/05, as applied to Claim 97, because the specification, while being enabling for pharmaceutical compositions comprising

neuronal cells, does not reasonably provided enablement for pharmaceutical compositions comprising glial cells”. In particular, the Office Action states that “nothing in Example 4...points to a therapeutic use...(and that)...[a]lthough donor mouse cells were detected in the rat brain following embryonic transplantation, no therapeutic effect was demonstrated.”

In order to facilitate prosecution, and not in acquiescence to the Examiner’s rejection, Applicants have canceled dependent claims 115, 125 and 134, and added new independent claims 137, 138 and 139. New claims 137, and 138 are drawn to pharmaceutical compositions comprising isolated non-tumorigenic cell compositions consisting essentially of embryonic stem cell-derived neural and glial precursor cells, and neuronal and/or glial cells derived from these embryonic stem cell-derived neural and glial precursor cells. New claim 139 is drawn to pharmaceutical compositions comprising isolated non-tumorigenic cell compositions consisting essentially of embryonic stem cell-derived glial precursor cells, and glial cells derived from these embryonic stem cell-derived glial precursor cells.

The Office Action states that, Applicants use of Example 4, demonstrating the effective transplantation of glial cells and/or precursors, and subsequent formation, of donor glial cell-derived myelin and astrocytes, is not adequate to provide “a therapeutic outcome”...(because)...”no therapeutic effect was demonstrated”.

Applicants respectfully disagree. A person of skill in the art would recognize that pharmaceutical/therapeutic application of the instant invention are fully supported by Applicants demonstration that the mouse embryonic stem cells transplanted into myelin-deficient recipient rats survived, developed and differentiated to form myelin-forming cells, as well as astrocytes, in the cortex, hippocampus, septum, striatum, bulbus olfactorius, thalamus, hypothalamus, tectum, cerebellum, corpus callosum, anterior commissure, tractus opticus and the optic nerve. One of skill in the art would recognize that the donor-induced formation and survival of myelin and astrocyte cells throughout the nervous system in such a myelin deficient host per se represents evidence of a therapeutic benefit to the recipient animal. Furthermore, although the study described in Example 4 was specifically designed to assess the histomorphological evidence for successful pre-glial cell transplantation, the findings are not inconsistent with a significant

beneficial affect on the myelin-deficiency phenotype (*i.e.*, the development of strong tremors by the third week of age and subsequent death within their fourth postnatal week). Accordingly, a person of skill in the art would recognize that the studies reported in the instant application do support a therapeutic benefit of the embryonic stem cell compositions of the invention.

Still further, strong evidence of a therapeutic effect has since been demonstrated in other studies using the method of the invention. Exhibit A, included with this Response, is a report demonstrating that such embryonic stem-cell derived oligodendrocyte progenitor cell transplants remyelinate and restore locomotion after spinal cord injury in rats (Keirstead, *et al.* (2005) J. Neurosci. 25: 4694-4705). Accordingly, the subsequent work of others, conducted after the filing of the instant application, has confirmed the therapeutic benefit of remyelination using the embryonic stem cell-derived compositions and methods of the instant invention.

Therefore, reconsideration and withdrawal of the rejection is respectfully requested.

**Rejections under 35 U.S.C. §112, 2nd<sup>d</sup> paragraph**

Claims 115, 125, and 134 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite in their recitation of “the precursor cells of” claims 106, 118 and (127), respectively, because each of these independent claims is directed to a cell composition and not precursor cells.

Applicants respectfully aver that the above-described cancellation of claims 115, 125, and 134, which have been amended and presented as new independent claims 137, 138 and 139, effectively obviates this rejection under 35 U.S.C. §112, second paragraph for lack of antecedent bases in the rejected dependent claims.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

**Rejections under 35 U.S.C. §102**

The Office Action further states that claims 106-136 have been rejected under 35 U.S.C. §102(e) as being anticipated by the Weiss *et al.* patent (U.S. Patent No. 5,980,885, hereinafter the '855 patent). In particular, the Office Action states that "[i]n the absence of evidence to the contrary, the (adult) neural stem cell compositions disclosed by Weiss *et al.* are indistinct from the cell compositions instantly claimed"... (and that)..."[t]he Declaration of Dr. Bruestle has been fully considered but is not found persuasive...(because)...[t]he presence of the purported less lineage-restricted neural precursor cells is not a limitation of the claims". Applicants disagree with this rejection for the reasons that follow.

As an initial matter, Applicants respectfully note that MPEP §2112 states that "[t]he fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic". (emphases added, citing *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993)). The same section of the MPEP goes on to instruct that "[t]o establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill...[i]nherency, however, may not be established by probabilities or possibilities...(and)...[t]he mere fact that a certain thing may result from a given set of circumstances is not sufficient'". (citing *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999)). MPEP §2112 concludes that "[i]n relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art". (citing *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).

Applicants respectfully aver that the Examiner has not provided a basis in fact and/or technical reasoning to support the contention that the embryonic and adult neural stem cell compositions taught by the '855 patent necessarily provides the improved, lineage-unrestricted cell compositions of the invention, and, further, that appropriate deference to the Second Declaration of Dr. Bruestle in this regard has not been given. The novel, lineage-unrestricted, pluripotent properties of the claimed invention are intrinsic to the claimed cell compositions and these properties are inherent to the teachings of the instant application.

Nevertheless, in the interest of facilitating prosecution of the application, and not in acquiescence to the rejection, Applicants have amended claims 106, 118 and 127 to clearly specify that the claimed cell compositions are regional-identity unrestricted, pluripotent cell compositions. Although Applicants believe this characterization of the novel properties of the claimed cell compositions was already inherently present in these product-by-process claims by virtue of the embryonic stem cell starting materials and explanatory Second Declaration of Dr. Bruestle, Applicants have amended these claims in this manner to address the Examiner's objection that "Applicants are arguing limitations that are not in the claims".

Therefore, in view of the proposed arguments and amendments to independent claims 106, 118 and 127, which thereby further apply to the rejected dependent claims 107-117, 119-126 and 128-136, Applicants respectfully request reconsideration and withdrawal of this rejection.

### CONCLUSIONS

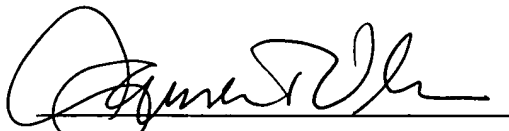
In view of the foregoing claim amendments and arguments presented, Applicants respectfully aver that the claims are in good condition for allowance, and reconsideration of the rejection and notification of such allowance is hereby respectfully requested.

Applicant encloses herewith a Petition for a Three Month Extension of Time up to February 14, 2007, along with a Request for Continued Examination under 37 C.F.R. §1.114 and this Amendment, in response to the Final Office Action dated August 14, 2006 and the Advisory Action dated February 12, 2007. Please charge our Deposit Account No. 08-0219 the \$225 fee (small entity) for this extension of time. Although no further fees are believed to be due at this time, please charge any other such fees due, or credit any overpayments, to Deposit Account No. 08-0219.

It has come to Applicant's attention that a copy of Form 1449 dated August 22, 2003 has not been returned with the Examiner's initials. Applicant respectfully requests that the Examiner review the art cited therein and return an initialed copy with the next action.

If the Examiner believes that a telephone conference would expedite this matter, the Examiner is respectfully requested to telephone the applicant's undersigned attorney at the number indicated below.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'James T. Olesen', written over a horizontal line.

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**Date: February 13, 2007**  
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